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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/911,777	07/24/2001	Jeffrey Browning	A070US	3867

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WASHINGTON, DC 20005

EXAMINER

HADDAD, MAHER M

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 08/27/2003

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/911,777

Applicant(s)

BROWNING ET AL.

Examiner

Maher M. Haddad

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 June 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10-13 and 16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10-13 and 16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 June 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 6/9/03 (Paper No. 14), is acknowledged.
2. Claims 10-13 and 16 are pending and under examination.
3. In view of the amendment filed on 6/9/03 (Paper No. 14), only the following rejections remained.
4. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
5. Claims 10-13 and 16 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the same reasons set forth in the previous Office Action, paper No. 13, mailed 3/11/03.

Applicant's arguments, filed 6/9/03 (Paper No. 14), have been fully considered, but have not been found convincing.

Applicant contends that the specification must be read in light of the knowledge of one of ordinary skill in the art as of the filing date of the application. Applicant asserts that a number of BAFF ligands from different species had been isolated, cloned, and sequenced, thus enabling the production and use of these molecules. Applicant further asserts that BAFF is a member of the TNF family of molecules, and that it shares a number of structural and functional characteristics with other TNF family members. Applicant concluded that it was well within the skill in the art at the time of filing to identify BAFF molecules in other species based on sequence and/or functional similarity with known BAFFs. Applicant argues that the identification and production of a homolg to a known protein is routine and requires no undue experimentation. Therefore, the specification provides an enabling disclosure of how to make and use any BAFF molecule or antigenic determinant thereof to practice the claimed methods.

Contrary to applicant assertion the specification provides only SEQ ID NO: 1 and SEQ ID NO:2. Regarding applicant's argument that claimed BAFF ligand is identify as a member of the TNF family. However, assignment of the claimed polypeptides to this family does not support an inference of enablement because the members are not known to share a common functional activity.

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Regarding applicant's argument that the specification provides a mouse and human example and substantial guidance on how to identify polypeptides other than human and mouse, the examiner notes that in order to satisfy the U.S.C 112, 1st paragraph, the specification has to teach how to make and/or use the invention, not how to identify the invention. Until the time when other BAFF sequences are identified, then one skill in the art can make them.

Regarding the efficacy of anti-BAFF antibody, Applicant asserts that the instant specification teaches that BAFF binds to B cells, induces B cell proliferation, induces immunoglobulin secretion, and can induce signaling in both naïve and mature B cells *in vitro*. Additionally, Applicant asserts that when overexpressed in transgenic mice, BAFF causes increased B cell populations; increased levels of immunoglobulins, rheumatoid factors, and circulating immune complexes; and lupus-like symptoms. Applicant argues that given the level of skill in the art relating to BAFF, the TNF family, and therapeutic antibodies, the instant specification provides ample disclosure of the claimed methods of treatment, enabling one skilled in the art to practice the invention without undue experimentation. Applicant provides an example on how to "synthesize antibodies", what types of antibodies to administer, and a variety of assays to their efficacy. Applicant submits that the specification provides ample guidelines for selection and use of appropriate antibodies, delivery methods, and dosages, in the claimed methods. Applicant submits that the specification provides a variety of assays to test the effectiveness of anti-BAFF antibodies on B cell proliferation and survival. Applicant argues that when such provisions are combined with the knowledge that antibody therapeutics have worked with respect to related proteins, and are specifically known to work for other TNF family members, one skilled in the art would not reasonably doubt the efficacy of the claimed methods.

However, the exemplification in the specification is drawn to stimulate B cell growth and immunoglobulin production using full length murine BAFF in BAFF Tg mice. Further, while applicant asserts that BAFF binds to B cells, induces B cell proliferation, induces immunoglobulin secretion, and can induce signaling in both naïve and mature B cells *in vitro*. Such *in vitro* assay may provide an indication that particular compounds/compositions are appropriate to target for *further experimental consideration*. Applicant's disclosure does not appear to have provided the skilled artisan with sufficient guidance and support as how to extrapolate data obtained from *in vitro* assay to the development of effective *in vivo* human therapeutic methods, commensurate in scope with the claimed invention. Furthermore, Applicant's *in vitro* assay uses directly the BAFF ligand rather than the claimed antibodies to BAFF ligand.

Further, results obtained under controlled conditions often differ from the clinical response obtained in patients. There is insufficient evidence or nexus that would lead the skilled artisan to predict the ability of the antibody specific for BAFF ligand to inhibit B- cell growth, immunoglobulin production or inhibiting dendritic cell-induced B-cell growth and maturation in an animal including human. Applicant's experimental results have relied on BAFF Tg mice. It is not clear that such model would reflect the therapeutic barriers presented by the treatment with anti-BAFF ligand in a clinical setting.

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There is insufficient guidance in the specification as to how to determine humans or animals in whom the inhibition of B-cell growth and/or immunoglobulin production is desired versus those in whom it is not desired.

Applicant argues that the use of an anti-BAFF antibody in ongoing clinical trials for the treatment of autoimmune diseases which demonstrates that BAFF antibodies do affect B cell proliferation and immunoglobulin production. Applicant submits that the synthesis and testing of particular antibodies now in clinical trials was within the skill of one skilled in the art and cannot be considered to be anything other than routine experimentation.

However, the Press Release "Human Genome Sciences initials trial of a new drug for systemic lupus erythematosus and other autoimmune disease" indicates that a Phase 1 clinical trial in patients. Phase I clinical trial encompasses bioavailability, pharmacokinetics, safety, dosing regimens and ranges, but no efficacy studies. Further, the evidence must be submitted in the appropriate form of a declaration. Unsupported data are not proper evidence, since they have not been peer-reviewed and their contents have not been attested under the appropriate declaration.

Consequently, without additional guidance in the specification, and the dearth of information in the art, for one of skill in the art to practice the invention as claimed, would require experimentation that is excessive and undue. The amount of guidance or direction needed to enable an invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art (In re Fisher, 427 F.2d 833, 839, 166 USPQ 18,24 (CCPA 1970)).

6. Claims 10-13 and 16 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action, paper No. 13, mailed 3/11/03.

Applicant's arguments, filed 6/9/03 (Paper No. 14), have been fully considered, but have not been found convincing.

Applicant submits that the claims are drawn to methods of using antibodies that recognize BAFF. Applicant argues that with human and murine BAFF sequences in hand, the skilled artisan is capable of identifying and cloning BAFF homologs from other species. Applicant contends that with this BAFF homolog, one skilled in the art would be able to make a therapeutically effective antibody that recognizes and binds to BAFF based on the teachings contained in the specification. Applicant further asserts that the specification provides descriptions of the methods of use of these antibodies.

However, the broad brush discussion of the skilled artisan is capable of identifying and cloning BAFF homologs does not constitute a disclosure of a representative number of members. No such homologs were made or shown to have activity. Only the polypeptides of SEQ ID NOs: 1

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and 2 are disclosed. The specification's general discussion of making and identifying for other species constitutes an invitation to experiment by trial and error.

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 10-13 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 8 of copending Application No. 10/214,065. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are drawn to the same or nearly the same method of inhibiting mature B-cell growth, inhibiting immunoglobulin production, co-inhibiting B-cell growth and immunoglobulin production, inhibiting dendritic cell-induced B-cell growth and maturation in an animal comprising administering an antibody specific for BAFF ligand or an fragment thereof. Specifically, since APBF is an APRIL subunit linked to BAFF subunit, then an antibody specific for APBF or an active fragment thereof, would recognize BAFF ligand of the instant claims. Furthermore, since APRIL and BAFF cytokines share the same cognate receptors (i.e. TACI and BCMA) and BCMA and TACI bind APRIL and BAFF with relatively high affinity, therefore an antibody against APRIL, BAFF or both would inherently accomplish the same method (see Ware CF. J Exp Med. 192(11):F35-8, 2000).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. Claim 16 stands rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 8 of copending Application No. 10/214,065 in view of Harlow et al (1989) for the same reasons set forth in the previous Office Action, paper No. 13, mailed 3/11/03.

Applicant requests that the rejection of claims 10-13 and 16 under double patenting be held in abeyance until allowable subject matter is found in one of the two applications.

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10. No claim allowed

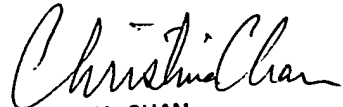
11. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9307.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
August 25, 2003


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